

## **REMARKS**

Reconsideration of this application, as amended, is respectfully requested.

Consideration and entry of this amendment is respectfully requested as it brings the application into condition for an allowance or in better form for consideration on appeal. The amendment does not raise any substantial new issues that would require any burdensome search by the Examiner.

### **A. Amendments to the Claims**

Claims 44-52 are pending in this application. Claims 70-72 have been cancelled without prejudice or disclaimer. New claims 73 and 74 have been added to more completely define Applicants' invention. Support for new claim 73 can be found in the application as originally filed at page 4, last paragraph – page 6, second full paragraph. Support for new claim 74 can be found in the application as originally filed in the paragraph bridging pages 10 and 11, page 11 in the first full paragraph, and at page 21, third paragraph – page 22, third paragraph. Accordingly, no new matter has been added to this application as a result of the new claims.

Claims 44, 48, 49, 51 and 52 were amended to clarify the invention. Support for all of the amendments can found in the application as originally filed. Claims 44, 49 and 51 have been amended to replace the term “multiepitope” with “multicomponent.” Support for these amendments can be found in the application as originally filed at page 5, fourth paragraph – page 6, third paragraph, as well as by the Examples, in particular, Example 1. As can be gathered from page 5, last paragraph – page 6, first paragraph, the use of analyte-specific receptors which bind to different epitopes of an analyte is just one specific embodiment of the invention; other embodiments, for example, are binding to different analyte sub-types or to sub-populations of an analyte. Claims 44, 49 and 51 have also been amended to change the “at least two epitopes” language to “at least two analyte-specific components.” Support for these amendments similarly can be found in the application as originally filed at page 5, fourth paragraph – page 6, third paragraph, as well as by the Examples, in particular, Example 1. Claims 44 and 49 have also been amended to make clear that the first and second receptors bind specifically with the analyte but to different analyte-specific components, wherein the first receptor binds specifically with a first analyte-specific component and the second receptor binds specifically with a second analyte-

specific component. Support for this amendment is found, for example, from original claim 1, wherein it is stated that different immobilized analyte-specific receptors are used, and also from the Examples. Additional support can also be found at page 23, last paragraph, which recites four receptors binding specifically with four different analyte-specific components as well as the relevant Table on page 25. It is because of the specific binding to different analyte-specific components that higher sensitivity and classification of the results, as shown in the Table on page 25, can be achieved at all. Only this, for example, enables distinction of the binding of the analyte to the different receptors, as shown in columns 3-6 in the Table at page 25 (entitled “p24, RT, gp41 peptide 1 and gp41 peptide 2). Claim 44 has also been amended to insert “one or more third receptors” that bind “specifically” to the analyte and are “directly or indirectly” bound to a signal generating group. Support for these amendments can be found at page 5, lines 8-10 and at page 5, lines 20-24. Claim 44 has also been amended to make clear in step (c) that the word “separately” refers to separate determination. Support for this amendment can be found in the Table on page 25 because only by separate determination and evaluation of the individual test areas can independent results be obtained for the different receptors. Claim 44 has also been amended to insert “at least” to receptor limitation. Support for this amendment can be found at page 5, line 4-6 (“and at least two spatially separate test areas, the test areas each containing different immobilized analyte-specific receptors”) and at page 5, lines 34-35 (“Each of the analyte-specific receptors immobilized on a test area is different”). Claim 49 has been amended to make clear that the analyte-specific component bound to the first test area is not simultaneously bound to the second test area. Support for this amendment to claim 49 can be found in Examples 2 and 3. If the analyte were not bound separately to the first test area (via a first analyte-specific component bound to the first receptor) and to the second test area (via a second analyte-specific component bound to the second receptor), the reported data could not have been generated; *i.e.*, differentiation between the individual test areas – which is indicative of binding of an anti-HIV antibody (the analyte) to an HIV antigen (the receptor) in that test area – would not be possible. Claims 48 and 52 have been amended to make clear that the detection reagent which is a universal detection reagent is a signal generating reagent. Support for this amendment can be found at page 5, lines 7-10. Accordingly, no new matter has been added to this application as a result of the amendments to the claims.

**B. Information Disclosure Statement**

The Action mailed September 22, 2005 indicates that Applicant's Information Disclosure Statement "filed 5/21/01" was received, entered and "considered by the examiner as indicated on the attached form PTO-1449." Applicants note that an Information Disclosure Statement was mailed September 13, 2005 (copy attached) and no form PTO-1449 accompanied the Action mailed September 22, 2005. Applicants respectfully request consideration of the references cited in the Information Disclosure Statement mailed September 13, 2005.

**C. Summary of the Invention**

In an effort to aid in the prosecution of this application, Applicants provide a concise summary of the claimed invention. The special feature of the invention is that different determinants are detected simultaneously, yet separately, for one analyte, e.g. a pathogen or a virus of an infectious disease. To this end, receptors of different analyte-specific determinants are applied in separate, spaced-apart test areas of a single analytic device. The different test areas are then all contacted with the same sample in one step, and the binding of the analyte to the different test areas containing the different receptors is measured via the respective analyte determinants. For example, in the case of determining HIV, which is a preferred embodiment of the invention (the invention, however, not being restricted to said pathogen), gp41 peptide 1, gp41 peptide 2, p24 and, if desired, further HIV antigens or HIV antibodies can be applied in separate test areas. The binding of the analyte, in this case HIV, to the different test areas takes place at different sites (e.g., epitopes) of the pathogen. The binding to the different determinant-specific receptors then can be evaluated individually. This is especially advantageous, if, for example, as in the case of HIV, different components or determinants, for example, antibodies or antigens indicating HIV, develop at different points in time. In this way, a progress of the occurrence of the different markers can be determined according to the invention, as also reflected by the Table on page 25, and at the same time a very early and sensitive detection of the pathogen is enabled.

Compared to the prior art, the invention offers considerably advantages, in particular,

higher sensitivity as well as the possibility of detecting diseases at a very early stage. This is the case, inter alia, because an optimal concentration of the respective receptors in the test areas can be adjusted by separate application of the individual determinant-specific receptors and no displacement reactions between the receptors themselves take place. Further, it is possible to adjust the cut-off value, i.e. the value distinguishing a positive from a negative signal, for a single determinant-specific receptor each. In case, for example, p24 epitope 1 and p24 epitope 2 are applied in separate test areas according to the invention, the background signal of p24 epitope 1 can be, for example, 100 mU, while the background signal of p24 epitope 2, for example, is 500 mU. When using a receptor mixture the cut-off value would have to be adjusted to at least 500 mU. If a signal of 300 mU were measured, this would be considered as a negative signal. According to the invention, however, a distinction could be made in that case between signals in area p24 epitope 1 and signals in area p24 epitope 2. A signal of 300 mU in area p24 epitope 1, for which a lower cut-off value of 100 mU could be fixed, thus, would indicate a positive signal, which would be left unnoticed when using a receptor mixture and not be realized as a positive signal.

Thus, the invention has clear advantages over the prior art, wherein receptor are applied as a mixture instead of separately in distinct test areas. Compared with embodiments wherein only one receptor is used, an improvement can be achieved according to the invention by using different receptors for the same analyte, especially for the same pathogen, whereby the receptors just bind to different components or determinants of the analyte, because different components of a pathogen are often present in a patient in different concentrations or are found at different points in time. The possibility of earlier detection of the pathogen is shown impressively in the Tables on page 25 and 27 of the present application. According to page 27, for example, HIV is detected at least one withdrawal (i.e. 2-3 days) earlier in the case of all test persons by means of the inventive procedure than by means of the combined Enzymun method, wherein the individual receptors are used as a mixture. Such early detection is possible, in part, because of the above-discussed possibility of the adjustment of the cut-off values.

**D. The Claims Are Supported by the Written Description**

Claims 44-48 stand rejected under 35 U.S.C. § 112 for failure to comply with the written description requirement. Applicants respectfully traverse the rejection.

The Office asserts that the amendment to claim 44 to recite a signal generating group that is bound separately to the first and second test areas via the analyte is not supported by the specification. Initially, Applicants note that claim 44 has been amended to re-locate the term “separately” in the claim to indicate that the determining step is performed separately in the test areas. Applicants respectfully submit that the specification fully provides support for this limitation. Claim 44 was previously amended to explicitly indicate that the claimed method is for simultaneous separate multiepitope (now multicomponent) detection, which requires that each test area be separately assayed for the signal generating group for the detection of the analyte in each separate test area. Applicants cited language at page 6 in the first full paragraph (“simultaneous separate detection”), at page 6 in the second full paragraph (“If a positive test is obtained on one or several, and in some cases on at least two test areas ...”), and at page 11 in the first full paragraph (“If several test areas are used which each allow the determination of different analyte molecules ...”) as support for these amendments. Applicants submit that the cited language does support the limitation that the signal generating group is bound separately to the first and second test areas via the analyte. If the signal generating group were not bound separately to the first and second test areas via the analyte, there could be no separate multicomponent detection in the first and second test areas; nor could there be several test areas which each allow the determination of different analyte molecules.

Applicants additionally point out the results presented in Examples 2 and 3 as providing support for the previous and current amendment to claim 44. If the signal generating group were not bound separately to the first test area via one molecule of the analyte bound to the first receptor and to the second test area via a second molecule of the analyte bound to the second receptor, Applicants submit that the reported data could not have been generated. The data in Examples 2 and 3 indicate that for any particular withdrawal, certain HIV receptors (in this case, HIV antigens) were able to bind the analyte (in this case, anti-HIV antibodies) while other HIV receptors were unable to bind the analyte. If the signal generating group were not bound

separately to the first and second test areas via the analyte, differentiation between the various test areas – which is indicative of binding of an anti-HIV antibody (the analyte) to an HIV antigen (the receptor) – would not be possible.

Moreover, Applicants submit that claim 44 as presently amended further clarifies that the claimed method achieves simultaneous separate multicomponent detection by allowing for the detection of the binding of an analyte to one test area via an analyte-specific component separately from the detection of the analyte bound to another test area via a different analyte-specific component. Since each test area of the invention separately binds a molecule of the analyte, claim 44 necessarily results in a signal generating group binding to each separate test area for simultaneous, separate detection of the analyte.

For the foregoing reasons, Applicants respectfully request withdrawal of the rejection of claims 44-48 under 35 U.S.C. § 112 for failure to comply with the written description requirement.

**E. The Claims Are Not Anticipated by Bellet *et al.***

Claims 49 and 51 stand rejected under 35 U.S.C. § 102(b) as being unpatentable over Bellet *et al.*, U.S. Patent No. 5,011,771 (hereinafter “Bellet”). Applicants respectfully traverse the rejection.

"A person shall be entitled to a patent unless ... the invention was patented or described in a printed publication in this or a foreign country ... more than one year prior to the date of the application for patent in the United States." 35 U.S.C. § 102(b). "For a prior art reference to anticipate a claim, the reference must disclose each and every element of the claim with sufficient clarity to prove its existence in the prior art." *E.g., Motorola, Inc., v. Interdigital Tech. Corp.*, 121 F.3d 1461, 1473 (Fed. Cir. 1997). Furthermore, the “statutory bar” to patentability of § 102(b) are evaluated on a claim-by-claim basis. *See e.g., Allen Eng’g Corp. v. Bartell Indus. Inc.*, 299 F.3d 1336, 1353 (Fed. Cir. 2002). Thus, to support a rejection based on anticipation by a 102(b) reference, the Office must point out where that reference discloses each and every element of a claim.

The Office asserts that Bellet teaches an immunometric assay comprising the formation of

a complex between antigen and multiple immobilized monoclonal antibodies against different epitopes of the antigen and with a detectably labeled monoclonal antibody. The Office also asserts that Bellet teaches a non-porous support with first and second spatially separate test areas with first and second analyte-specific receptors, and direct the Applicants to Figures 1B-1D as support. As discussed in previous Responses, the Applicants respectfully disagree that Bellet teaches first and second *spatially separate* test areas, each test area containing only one type of analyte-specific receptor. Bellet notes that the “assay was developed when a *mixture* of AF01 and AF03 were used on the solid phase support ...” Col. 12, lns. 63-65 (emphasis added); *see also* col. 11, lns. 58-63. Since Bellet describes a procedure wherein a receptor mixture is applied, Bellet does not teach a single type of an analyte-specific receptor per test area. In fact, it is the use of a mixture which is the unique aspect of Bellet because only by the binding of two receptors that a third binding site is generated (cf. Col. 2, lines 44-66; col. 4, lines 40-47; col. 8, lines 7-9).

Because Bellet does not teach the separate application of different analyte-specific receptors in different test areas but rather application of a mixture, separate evaluation of the individual test areas, which is the very improvement intended by the invention, is not possible. Bellet does not teach that test areas are formed, wherein one single receptor is applied each; instead, Bellet requires at least two different receptors to achieve the desired effect – creating the third binding site needed for detection. Moreover, evaluation of the results of the individual test areas, as provided by the present invention, is not possible, if a surface provided with mixed receptors is present and each of said receptors would be considered as a single test area. In addition, it is not clear how one single signal could be measured for each receptor if the test areas are defined by the Office because high resolution systems necessary for such detection are not available. Thus, the solid phase support in Bellet contain only a *single* test area containing more than one type of analyte-specific receptor, and for this reason cannot anticipate claims 49 and 51.

Moreover, claim 49 (and claim 51 since it incorporates the solid phase according to claim 49), as amended, makes clear that the first receptor binds specifically with the analyte via a first analyte-specific component and the second receptor binds specifically with the analyte via the second analyte-specific component, and that the analyte-specific component bound to the first test area does not simultaneously bind to the second test area. The Office notes that Bellet “discloses

an immunometric assay comprising the formation of a complex between antigen and multiple immobilized monoclonal antibodies against different epitopes of the antigen.” However, Bellet does not teach the binding of the first receptor with the analyte via a first analyte-specific component and, separately, the binding of second receptor with the analyte via the second analyte-specific component. In addition, Bellet does not teach that the analyte-specific component bound to the first test area is not simultaneously bind to the second test area. Since Bellet does not teach these limitations, Bellet does not anticipate claims 49 and 51. Therefore, Applicants respectfully request withdrawal of the rejection of these claims over Bellet.

**F. The Claims Are Not Anticipated by Linsley *et al.***

Claims 44, 47, 49 and 51 stand rejected under 35 U.S.C. § 102(e) as being unpatentable over Linsley *et al.*, U.S. Patent No. 6,004,761 (hereinafter “Linsley”). Applicants respectfully submit that Linsley fails to teach all of the limitations of the rejected claims and thus, cannot anticipate these claims.

Linsley describes new monoclonal antibodies reactive with mucins, wherein 14 new monoclonal antibodies are described (cf. column 2, lines 33-62). Thereby individual binding of these antibodies to mucins is described using a double determinant immunoassay (DDIA). Linsley describes an assay in which a first antibody is immobilized on a solid phase, then treated with the sample and thereafter bound with a second antibody which is labelled (cf. column 3, line 66 to column 4, line 17). The designation “double determinant”, thus, refers to the use of two antibodies in the sense of a sandwich assay for the detection of a analyte, whereby one determinant is used for binding to a solid phase via a first antibody and a second determinant for attaching a label via a second antibody. Further, it is stated that the second labeled antibody, if necessary, should also bind to a different epitope than the first antibody (cf. column 4, lines 17-30). What is not described by Linsley, however, is the method of the invention, wherein different analyte-specific receptors are applied onto one solid phase in different test areas. In the Examples in Linsley, only one antibody is immobilized on a solid phase, e.g. Onc-M26 or Onc-M29 (cf. column 17, line 58), as capture antibody. Thus, Linsley does not teach a solid phase with at least a first and a second receptor, the first and second receptors binding specifically with said analyte but to different analyte-specific components (claim 44) or a solid phase with a first and a second



receptor, the receptors binding specifically to the analyte but to different components epitopes of the analyte (claim 49). Because Linsley does not teach all of the limitations of claims 44 or 49, Linsley cannot anticipate claim 44, 47, 49 or 51. Therefore, Applicants respectfully request withdrawal of the rejection.

**F. The Claims Are Not Obvious from Bellet *et al.* in view of Kuo**

Claims 50 and 52 stand rejected under 35 U.S.C. § 103 as being unpatentable over Bellet in view of Kuo, EP 0 813 064. Applicants respectfully traverse the rejection.

A claimed invention is unpatentable if the differences between it and the prior art “are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art.” 35 U.S.C. § 103(a); *see Graham v. John Deere Co.*, 383 U.S. 1, 14 (1966). As noted by the Office, the ultimate determination of whether an invention is or is not obvious is based on underlying factual inquiries including: (1) the scope and content of the prior art; (2) the level of ordinary skill in the prior art; (3) the differences between the claimed invention and the prior art; and (4) objective evidence of nonobviousness. *See Graham*, 383 U.S. at 17-18.

The MPEP clearly provides the criteria for establishing a *prima facie* case of obviousness: (1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings, (2) there must be a reasonable expectation of success, and (3) the prior art reference (or references when combined) must teach or suggest all the claim limitations. MPEP § 2142. The obviousness inquiry set forth in *Graham* focuses on whether the prior art as a whole teaches, suggests, or motivates one of ordinary skill in the art to make the invention and whether the skilled artisan would have a reasonable expectation of making and using it. *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991). The suggestion, teaching, or motivation to combine may flow from the prior art references themselves, the knowledge of one of ordinary skill in the art, or, in some cases, from the nature of the problem to be solved. *See Pro-Mold & Tool Co. v. Great Lakes Plastics, Inc.*, 75 F.3d 1568, 1573 (Fed. Cir. 1996).

In this case, that the prior art (Bellet in combination with Kuo) fails to teach or suggest all of the elements of claims 50 and 52. Thus, Applicants respectfully submit that the Office has

failed to establish a *prima facie* case of obviousness as these claims. Applicants also submit that the Office establish cannot a *prima facie* case of obviousness of these claims in view of the present amendments to claims 49 and 51.

The Office asserts that Bellet teaches an immunometric assay comprising the formation of a complex between antigen and multiple immobilized monoclonal antibodies against different epitopes of the antigen and with a detectably labeled monoclonal antibody. While the Office concedes that Bellet does not teach the diameter of the test area, a control area (although this appears to be in error, since neither of the rejected claims contain this limitation) or latex particles as the label, the Office asserts that the control area and the latex particles are taught by Kuo and that the diameter of the test area simply represents an optimization of the assay. Applicants respectfully disagree that all of the claim limitations of these claims are taught in or obvious from the prior art. Claim 50 depends from claim 49 and claim 52 depend from claim 51. For the reasons discussed above for anticipation, Applicants believe that Bellet fails to teach first and second *spatially separate* test areas, each test area containing only one type of analyte-specific receptor. Nothing in Kuo teaches or suggests this limitation.

Moreover, Applicants respectfully submit that the present amendments to claims 49 and 51 obviate the obviousness rejection of claims 50 and 52. Bellet does not teach that the first receptor binds specifically with the analyte via a first analyte-specific component, that the second receptor binds specifically with the analyte via the second analyte-specific component, and that the analyte bound to the first test area (via the first analyte-specific component) does not simultaneously bind to the second test area. These claim limitations are likewise not taught or suggested by Kuo. Because Bellet in view of Kuo do not teach or suggest all of the limitations of claims 50 and 52, these claims are not obvious. Applicants respectfully request withdrawal of the rejection.

**G. The Claims Are Not Obvious from Linsley *et al.* in view of Mehta *et al.***

Claims 45-46 and 50 stand rejected under 35 U.S.C. § 103 as being unpatentable over Linsley in view of Mehta *et al.*, U.S. Patent No. 5,173,399 (hereinafter “Mehta”). Applicants respectfully traverse these rejections.

First, the Office has failed to identify how the cited art teaches each and every limitation of the claims. For the reasons discussed above in the anticipation rejection based on Linsley, that reference fails to teach all of the limitations of the underlying independent claims (claims 44 and 49). The Mehta reference does not cure this deficiency – it does not teach a solid phase with at least a first and a second receptor, the first and second receptors binding specifically with said analyte but to different analyte-specific components (claim 44) or a solid phase with a first and a second receptor, the receptors binding specifically to the analyte but to different components epitopes of the analyte (claim 49). Since all of the limitations of claims 45, 46 and 50 are not taught by Linsley in view of Mehta, these claims cannot be rejected as obvious in view of these references.

Second, the prior art does not provide a *particularized* suggestion or motivation to make the claimed invention. The Office has failed to identify where in the cited art there is a suggestion to combine the analytes recited in the present claims into the method or into a single composition in the manner described in the claims. The Office concedes that Linsley fails to teach a method wherein the analyte is selected from the group consisting of HIV I, HIV II, HBV and HCV-antibodies and HIV antigens. The Office thus cites Mehta for its teaching of anti-HIV p24 antibodies. The Office then asserts that it would have been obvious of one of skill in the art to use the antibodies of Mehta in the method of Linsley to arrive at the methods and solid phase claimed in claims 45, 46 and 50. But the Office never alleges that Linsley or Mehta provide the requisite suggestion to combine all the limitations of the present claims.

The law requires that the suggestion or motivation that forms the basis of an obviousness rejection be particularized, directed to the invention being claimed; a general motivation or suggestion is simply insufficient. This exact proposition was directly addressed by the Federal Circuit in *In re Lee*, 61 USPQ2d 1430, 1432 (Fed. Cir. 2002), where the court flatly rejected the Patent Office Board of Patent Appeals position that “The conclusion of obviousness may be made from common knowledge and common sense of a person of ordinary skill in the art without any specific hint or suggestion in a particular reference.” The court stated

When patentability turns on the question of obviousness, the search for and analysis of the prior art includes evidence relevant to the finding of whether there is a teaching, motivation, or suggestion to select and combine the references relied on as evidence of obviousness. The factual inquiry whether to combine references must be thorough and searching. It must be based on objective evidence of record. This precedent has been

reinforced in myriad decisions, and cannot be dispensed with. The need for specificity pervades this authority.

*Id.* at 1434 (citations omitted). *See also In re Deuel*, 34 U.S.P.Q.2d 1210, 1215 (Fed. Cir. 1995) (the prior art must suggest the particular form of the invention and how to make it; general guidance is insufficient); *In re Rouffet*, 47 USPQ2d 1453, 1459 (Fed. Cir. 1998) (“even when the level of skill in the art is high, the Board must identify specifically the principle, known to one of ordinary skill, that suggests the claimed combination. In other words, the Board must explain the reasons one of ordinary skill in the art would have been motivated to select the references and to combine them to render the claimed invention obvious.”); and *In re Obukowicz*, 27 U.S.P.Q.2d, 1063, 1065 (Bd. Pat. App. Int. 1992) (Prior art “that gives only general guidance and is not at all specific as to the particular form of the claimed invention and how to achieve it . . . does not make the invention obvious.”).

The Applicants respectfully submit that the Office has failed to identify in the prior art any suggestion or motivation to use a method for simultaneous separate multiepitope detection of an analyte in a sample wherein the analyte is selected from the group consisting of HIV I, HIV II, HBV and HCV-antibodies and HIV antigens. Nor has the Office identified in the prior art any suggestion or motivation to make a solid phase for simultaneous separate multiepitope detection of an analyte in a sample wherein the analyte is selected from the group consisting of HIV I, HIV II, HBV and HCV-antibodies and HIV antigens. Rather, the Office has identified (some, but not all) elements of the present claims scattered throughout Linsley and Mehta without identifying specific teachings to bring all the elements together. The Applicants respectfully submit that this amounts to nothing more than hindsight reconstruction of the present claims.

Without a particularized suggestion or motivation to make the claimed invention, the obviousness rejection of claims 45, 46 and 50 cannot stand. Nor can this obviousness rejection be applied to any of the claims as amended.

#### **H. The Claims Are Not Obvious from Linsley *et al.* in view of Valkirs *et al.***

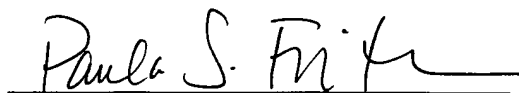
Claims 46, 48, 50 and 52 stand rejected under 35 U.S.C. § 103 as being unpatentable over Linsley in view of Valkirs *et al.*, U.S. Patent No. 6,348,318 (hereinafter “Valkirs”). Applicants respectfully traverse the rejection.

Claims 46 and 48 depend from claim 44, claim 50 depends from claim 49 and claim 52 depend from claim 51 (which incorporates all of the limitations of claim 49). As discussed above in addressing the anticipation rejection based on Linsley, that reference fails to teach all of the limitations of the underlying independent claims. The Valkirs reference does not cure this deficiency – it does not teach a solid phase with at least a first and a second receptor, the first and second receptors binding specifically with said analyte but to different analyte-specific components (claim 44) or a solid phase with a first and a second receptor, the receptors binding specifically to the analyte but to different components epitopes of the analyte (claim 49). Since all of the limitations of claims 46, 48, 50 and 52 are not taught by Linsley in view of Valkirs, these claims cannot be rejected as obvious in view of these references. In addition, as with the obvious rejection based on Linsley in view of Mehta, the Office has failed to point out where the references provide the motivation to combine the teachings. Instead, the Office has again pieced together parts of the disclosures of Linsley and Valkirs to arrive at what is asserted to be the claimed invention. This hindsight reconstruction must fail in the absence of any indication that the references provide any motivation to combine. For the foregoing reasons, Applicants respectfully request withdrawal of the rejection.

**I. Conclusion**

In view of the amendments and remarks above, the application is considered to be in proper form for allowance. Therefore, the Office is respectfully requested to pass the application to issue. If the Office is of the opinion that a teleconference would expedite the prosecution of the application, the Examiner is encouraged to contact Applicant's undersigned representative.

Respectfully submitted,



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